of c-*myc*, *ras*, and p53 [4]. We postulate that recurrent pericarditis caused sustained or intense stimulation through the excessive production of antigens and played an important role in the lymphomagenesis. The association between pericarditis and Burkitt's lymphoma has not been reported hitherto. Interestingly, Zweiker et al. [5] recently described a 28-year-old woman with *Toxoplasma* perimyocarditis preceding T-cell non-Hodgkin's lymphoma.

It would be of interest to evaluate prospectively high-grade lymphoma patients for the presence of various pathogens (other than EBV, HIV, or malaria) causing chronic antigenic stimulation. Such careful clinical evaluation could provide important clues for the identification of additional factors required to promote tumor progression.

Our patient was treated with chemotherapy, followed by autologous bone marrow transplantation and immunotherapy. Following this intensive treatment, the cells and organ systems have changed in a way that makes them more susceptible to previous etiological factors and, possibly, in this case recurrent pericarditis. Therefore, future follow-up evaluation of this case will be of great interest.

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Chronobiological Circadian Aspects of Serum Lactate Dehydrogenase and Serum Thymidine Kinase in Monitoring Multiple Myeloma

To the Editor: In the field of oncology, the most important aim to date has been the findings of new means to improve the diagnosis, the monitoring, and the prognosis of neoplastic diseases. For these purposes, clinical chronobiology is searching for potential circadian marker rhythms that could be used to study the various clinical phases of cancer diseases.

In multiple myeloma (MM), the serum levels of lactate dehydrogenase (sLDH) and the serum levels of thymidine kinase (sTK) are considered markers of the enzyme activity of the proliferating bone marrow plasma cells; they seem to be very reliable parameters for estimating prognosis and for monitoring the disease [1]. Since oscillation is a fundamental characteristic of all living systems [2], the chronobological approach to this study attempts to find some quantitative and qualitative circadian changes in sLDH and sTK values, useful not only in diagnosis, but also in monitoring multiple myeloma, capable of detecting its clinical phases, such as active disease, remission, and relapse.

Four groups of subjects were considered for this study: group A, six male adult clinically healthy subjects as controls; group B, six male adult previously untreated MM patients; group C, six male adult MM patients in complete remission (reduction >75% of initial total body myeloma cell mass), after chemotherapy with melphalan plus prednisone; and group D, six male adult MM patients in relapse, after complete or partial remission (reduction >50% of initial total body myeloma cell mass). All patients met the diagnostic criteria for MM according to the Southwest Oncology Group; they were in II or III clinical stages, and they were not affected by liver disease.

After 1 week of standardized life conditions in hospital, with meals at 8:30 AM, 12:30 PM, and 6:30 AM, sleep and/or rest period from 10:00 PM to 6:00 AM, without any therapy, venous blood samples were drawn from a peripheral vein every 4 hr, starting from midnight, during the span of a whole day, for the determination of total sLDH enzyme activity (U/L) by spectrofotometric method and for total sTK enzyme activity (U/L) by radioenzyme assay.

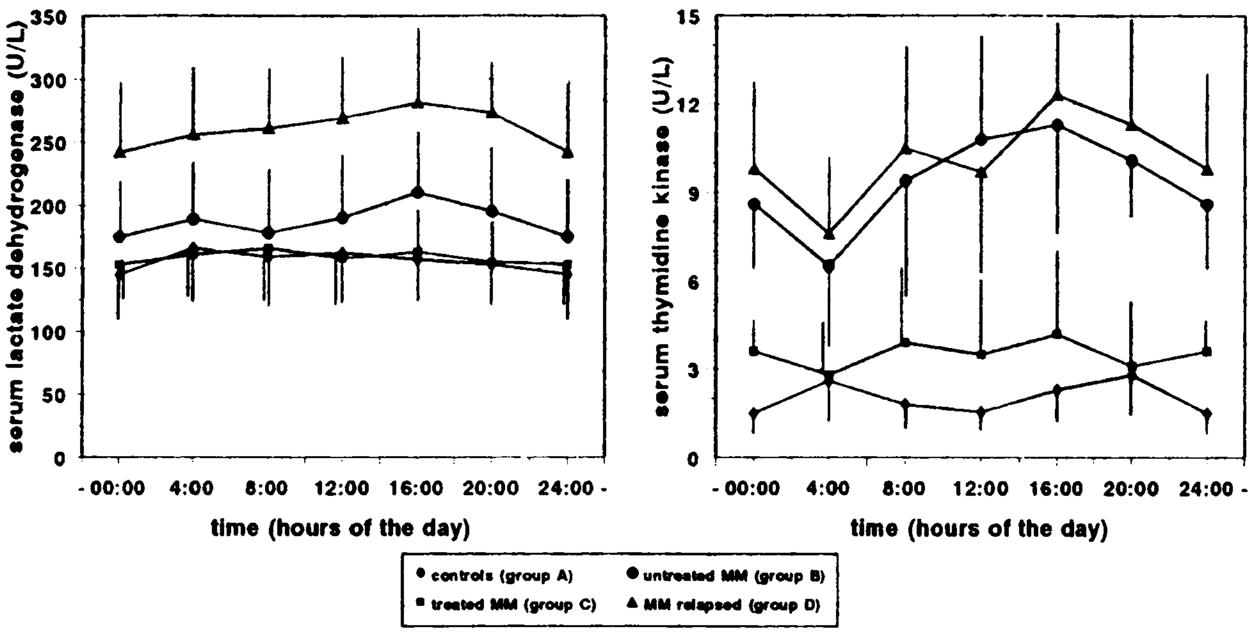
The time-related values of sLDH and sTK were subjected to statistical analysis using chronograms (mean ± 1SD) and to inferential circadian statistical analysis by means of the "mean-group cosinor" method [3], which is able to detect a significant ($P < 0.05$) circadian rhythm and the rhythm parameters: mesor (average level of rhythm), amplitude (length from mesor to acrophase), and acrophase (peak of rhythm). The circadian rhythms of sLDH and sTK were compared among the four studied groups by the "Hotelling's statistic test" [3].

The circulating sLDH and sTK levels fluctuated during the day in all groups. When the same data were analyzed by the "mean-group cosinor" method, significant ($P < 0.05$) circadian rhythms were demonstrated for the untreated MM patient (group B) and for MM patients in relapse (group D); no rhythms were detected in the other groups (Fig. 1). The highest values of sLDH and sTK in untreated MM patients and in relapsed MM patients have been observed in the afternoon. Significant ($P < 0.05$) differences were noted in sLDH and sTK circadian rhythms between controls and the other groups studied, between untreated MM patients and MM patients in remission, and between MM patients in remission and MM patients in relapse.

Several variables have been investigated and proposed as circadian marker rhythms in MM, such as serum iron, Bence-Jones proteinuria, serum monoclonal component, serum calcium, hydroxyprolinuria, β_2-microglobulin, C-reactive protein, phosphoexoseisomerase enzyme activity, and others [4,5].

Our data suggest that significant modifications in the circadian rhythms of sLDH and sTK occur in patients with MM, and the changes seem to be due to the effect of therapy. Comparison among the groups shows that the values in mesors and amplitudes of the two enzymes in treated patients are lower in respect to untreated and to relapsed patients and that they return to the normal range during complete remission. The presence of significant sLDH and sTK circadian rhythms in untreated MM patients could indicate that the activity of myeloma cells has its own circadian rhythm, reaching a maximum in the afternoon. This hypothesis seems to be confirmed by the observation that the relapsed patients present the same sLDH and sTK circadian rhythms. Moreover, it is worth noting that a similar circadian pattern has been observed in untreated and treated MM patients for many other variables [2,4,5] that estimate myeloma cell activity. In other words, the presence of significant circadian rhythms for sLDH and sTK values in untreated and relapsed MM patients seems to be due to a synchronization in neoplastic activity. Thus, the relative loss of the two circadian rhythms in treated patients could be related to the cell neoplastic activity and to the effect of therapy that inhibits proliferation; this could modify in some way the biological time structure of the neoplastic plasma cells. Successively, during relapse, there is a progressive return to circadian patterns of sLDH and sTK similar to those preceding the remission, as well as it occurs regarding the enzyme phosphoexoseisomerase [5] and β_2-microglobulin [2].

In conclusion, chronobiological circadian study of these two markers could (1) reflect the characteristics of myeloma cell growth, (2) be important



Variable	group	PR	p	mesor (SE)	amplitude (95%CL)	acrophase (95%CL)	time (95%CL)
	A	50	>0.05	157.0 (3.7)	0.7 (- # -)	-140° (- # -)	9:20 AM (- # -)
sLDH	B	57	<0.05	189.5 (5.3)	12.3 (0.1#24.5)	-243° (-187°#-299°)	4:12 PM (12:28 PM # 7:56 PM)
(U/L)	C	53	>0.05	159.6 (4.7)	4.6 (- # -)	-145° (- # -)	9:40 AM (- # -)
	D	71	<0.02	263.5 (6.6)	15.4 (5.2#25.6)	-224° (-186°#-262°)	2:56 PM (12:24 PM # 5:28 PM)
	A	26	>0.05	2.08 (0.27)	0.19 (- # -)	-317° (- # -)	9:08 PM (- # -)
sTK	B	78	<0.03	9.45 (0.38)	2.13 (1.31#2.95)	-228° (-202°#-254°)	3:12 PM (1:28 PM # 4:56 PM)
(U/L)	C	46	>0.05	3.52 (0.33)	0.37 (- # -)	-207° (- # -)	1:48 PM (- # -)
	D	66	<0.04	9.98 (0.48)	2.70 (1.34#4.06)	-249° (-203°#-295°)	4:36 PM (1:32 PM # 7:40 PM)

PR = percentage of rhythm; 95%CL = confidence limits at 95% of probability.

Fig. 1. Diurnal fluctuations (mean ±1 SD) of serum lactate dehydrogenase (sLDH) and serum thymidine kinase (sTK) levels in the four studied groups and results of the "mean-group cosinor" analysis.

in programming a treatment scheme according to time, and (3) be a new and useful approach for monitoring patients with MM.

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Atypical Follicular Hyperplasia With Clonal Rearrangement for Immunoglobulin and T-Cell Receptor Genes: Biclonal Proliferation of B Cell and T Cell

To the Editor: Angioimmunoblastic lymphadenopathy with dysproteinemia (AILD) [1,2] and immunoblastic lymphadenopathy (IBL) [3] can best be described as disorders of T cells resulting in polyclonal B-cell proliferation. Pathological findings of the involved lymph nodes include prominent obliteration of the nodal architecture with capsular infiltration, vascular prolifera-